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10/027,484	12/21/2001	Sebastian Bohm	TGZ-001B	9951

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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/027,484	BOHM ET AL.
	Examiner	**Art Unit**
	Jeffrey T. Barton	1753

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45,47-64 and 66-70* is/are pending in the application.

4a) Of the above claim(s) *2-8,22-41,49-54,59,60 and 67-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-21,42-45,47,48,55-58,61-64,66 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 October 2005 has been entered.

Response to Amendment

2. The amendment filed on 19 October 2005 does not place the application in condition for allowance.

Status of Objections and Rejection Pending Since the Office Action of 19 April 2005

3. All objections and rejections of claims 46 and 65 are obviated due to cancellation of the claim.

4. All other previous rejections are maintained.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 9-19, 42-45, 47, 48, 55-58, 61-63, 66, and 70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims include a limitation to a port having "a diameter that is significantly larger than the depth so as to minimize a total volume of the fluid interface port". It is unclear how having a diameter specifically *larger* than the depth minimizes this volume.

Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1, 42, 47, 48, 56-58, 61-64, 66, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al (WO 99/64850) in view of either McCormick et al or Amigo. Since WO 99/64850 is in German, citations below are given to US Patent No. 6,846,398, which issued from the National Stage entry of this International Application.

Regarding claims 1, 42, 64, 66, and 70 Heller et al disclose a method of injecting a second liquid into a microchannel filled with a first liquid comprising: forming a droplet from the second liquid and directing the droplet to, and introducing it through a virtual wall formed by the first fluid in a fluid interface port (Figure 2, port A) formed in a sidewall of the microchannel. (Column 6, lines 1-28; menisci that inherently form at the

areas A after filling with buffer correspond to the "virtual walls") The menisci of the first liquid lie in a plane shared by the sidewall and can therefore be described as "substantially coplanar". Heller et al disclose ports A with diameters of 20 - several hundred microns. (Column 4, lines 61-62; Column 6, lines 1-2; ports are shown as being as wide as the channels in Figure 2) The ports must inherently have a depth equal to the thickness of the sidewall.

Regarding claim 48, Heller et al disclose the droplet traversing the virtual wall. (Column 6, lines 20-28; inherent in the loading step) As such, its speed and direction must be appropriate.

Regarding claims 56 and 57, Heller et al disclose motion of the injected fluid in the microchannel, due to an applied electric field. (Column 6, lines 29-33)

Regarding claim 58, Heller et al disclose application of droplets with volume as low as 100 pL. A spherical 100 pL droplet has a diameter of approximately 12 microns, well below the disclosed port diameter.

Regarding claims 61 and 62, Heller et al disclose forming the droplet on, and applying it to the loading port, via a droplet carrying element. (Column 6, lines 20-28)

Relevant to claim 63, Heller et al disclose applying several droplets and applying each to a different port. (Column 6, lines 25-28, Figures 1 and 2)

Heller et al do not explicitly describe the dead volume within the interface ports, nor do they explicitly describe the ports as having a diameter significantly larger than their depth. Heller is silent concerning the thickness of the cover plate.

Amigo discloses similar microfluidic systems, which use a cover having a thickness as low as 10 microns. (Column 8, lines 1-6)

McCormick et al disclose a microfluidic system in which they cover the channels with a cover as thin as 10 microns. (Column 13, lines 17-22)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Heller et al by performing it in a device wit a cover plate of 10 micron thickness, as taught by either Amigo or McCormick et al, because the silence of Heller et al concerning this indicates that a skilled artisan could choose any suitable cover thickness, such as those known in the prior art, e.g. McCormick et al or Amigo. The choice of thinner material could be motivated by reduction of material consumption, which could potentially reduce manufacturing costs.

Regarding the limitations to specific dead volumes, the dead volume is simply a function of the affinity of the fluid within the channel for the walls of the port, fluid surface tension, and the respective pressures of the liquid and gas at the interface. There is nothing to physically distinguish the port of this combination from that described in the instant specification.

9. Claims 1, 42, 47, 48, 56, 58, 63, 64, 66, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al.

Regarding claims 1, 42, 64, 66, and 70, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first liquid (Figure) comprising: forming a droplet from the second liquid (Figure, droplet 5) and directing the droplet to, and introducing it through a virtual wall formed by the first fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9). (Column 2, line 65 - Column 3, line 34) The meniscus of the first liquid lies in a plane shared by the sidewall (Thin section of FMD chip 1), as shown in the Figure, and can therefore be described as "substantially coplanar".

Regarding claim 48, Howitz et al disclose the droplet traversing the virtual wall. (Column 3, lines 31-34) As such, its speed and direction must be appropriate.

Regarding claim 56, Howitz et al disclose fluid motion in the microchannel. (Column 2, lines 1-37)

Regarding claim 58, Howitz et al disclose a droplet having a diameter smaller than the fluid interface port. (Figure)

Relevant to claim 63, Howitz et al also suggest introduction of plural fluids through the interface ports of their device. (Column 1; repeated mention of a fluid microdiode permeable to *fluids* (italics added))

Regarding claim 64, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first fluid, said method comprising: forming a droplet (5) from the second liquid, introducing said droplet through a virtual wall formed by the first

fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9), said fluid interface port having a diameter between about 25 µm and about 100 µm. (Column 2, line 65 - Column 3, line 34)

Howitz et al do not explicitly describe the dead volume within the interface ports or the introduction of a second droplet of a third fluid through a virtual wall in a second interface port, nor do they explicitly describe the ports as having a diameter significantly larger than their depth.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz by performing it in a device wherein the interface port has no dead volume (Claim 47) or dead volume of less than a picoliter (Other claims), because this dead volume is simply a function of the affinity of the fluid within the channel for the walls of the port, fluid surface tension, and the respective pressures of the liquid and gas at the interface. Howitz discusses such variability of meniscus formation (Column 3, lines 25-31), and choice of fluids, pressures, and materials would allow minimization or elimination of the dead volume.

In addition, regarding the limitation that the port has a diameter larger than its depth, although the example given by Howitz et al does not meet this limitation, Howitz et al also disclose variation of the depth of the port. (i.e. length of the capillary; Column 2, lines 5-10 and 27-30) Choice of a shorter length such that this limitation is met would have been obvious to a skilled artisan, particularly given the trend toward miniaturization in this art. Regardless, such limitations directed solely to relative dimensions cannot be held to distinguish claims from the prior art. In *Gardner v. TEC Systems, Inc.*, 725 F.2d

1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

Regarding claim 63, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to use the invention of Howitz et al for the introduction of plural fluids to the fluid-filled channel, because it is suggested by Howitz et al and combination of multiple fluids is a common process requirement.

10. Claims 9-12, 14, 15, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) in view of Bjornson et al.

Relevant to claim 9, Columbus discloses a method of filling a microchannel, comprising directing fluid droplets through an interface port in the channel sidewall (Column 13, lines 30-34), such that the liquid traverses the port and enters the interior. (Column 13, line 42 - Column 14, line 16) The port has a depth equal to the thickness of the sidewall. (Figures)

Relevant to claim 10, Columbus discloses the port being a filling aperture. (Column 13, lines 66-68)

Relevant to claims 11 and 12, Columbus discloses a pressure barrier formed in the microchannel to force the liquid in a first direction. (Figure 19, wider zones 220 force

fluid to fill narrower portions of the channel) These widened portions can be called, "stopper holes."

Relevant to claim 14, Columbus discloses vent holes through the sidewall. (Column 14, lines 59-68)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figures 20a-c; Column 14, lines 22-40)

Relevant to claim 20, Columbus discloses filling the channel with two fluids introduced into separate filling apertures, each according to the method of claim 9. (Figures 20 a-c; Column 13, line 30 - Column 14, line 16) The sidewall of Columbus (e.g. Figure 2, plate 38) encompasses a hollow interior having a dimension (which reads on "diameter", since the channels are not limited to a circular shape) as low as 60 microns. (Column 7, lines 20-25)

Relevant to claim 21, Columbus discloses introduction of a gelatinous solution that would not be miscible with an introduced sample fluid. (Column 10, lines 4-41)

Columbus does not explicitly disclose a fluid interface port having a dead volume of less than a picoliter (Claims 9-12, 14, and 15), nor does he explicitly disclose the filling apertures (e.g. 27) having diameters substantially equal to the "diameter" of the hollow interior.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with

diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters. The range of orifice diameters preferred by Bjornson et al (Column 11, lines 54-64) includes the microscale dimensions the device of Columbus (Column 7, lines 20-25), and match typical channel dimensions within the system of Bjornson et al. (Column 8, line 64 - Column 9, line 4)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Columbus et al by using thinner plate materials and smaller port diameters that substantially match channel dimensions, as taught by Bjornson et al, because miniaturization of these devices (Columbus is directed to electrochemical analysis of biological fluids) would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

Specific to claims 20 and 21, selection of a suitable port size would have been a matter of choice to one having ordinary skill in the art.

Whether the port diameter is substantially larger than its depth is a function of the thickness of plate materials and port diameter, selection of which lies within the level of ordinary skill in the art. Applicants' amendment relies upon recitations of relative size as bases for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ

777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

11. Claims 9, 10, 14, 15, 42, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,426,451) in view of Bjornson.

Relevant to claim 9, Columbus discloses a method of filling a microchannel (Figures 1 and 2), comprising directing fluid droplets through an interface port in the channel sidewall (Column 5, lines 24-28), such that the liquid traverses the port and enters the interior. (Column 4, line 55 - Column 5, line 43) The port has a depth equal to the thickness of the sidewall. (Figures)

Relevant to claim 10, Columbus discloses the port being a filling aperture. (Column 5, lines 24-28)

Relevant to claim 14, Columbus discloses vent holes through the sidewall. (Figure 2, hole 50)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figure 2, channel 22 is filled)

Relevant to claim 42, Columbus discloses introduction of a second fluid into a microchannel filled with a first fluid by directing a second liquid to a virtual wall formed in an interface port by the first fluid. (Figures 2-3; Column 7, lines 59-60) The meniscus of

the fluid within the channel forms in a plane defined by the sidewall (Figure 2), therefore it can be said to be "substantially coplanar" with the sidewall.

Relevant to claim 55, Columbus discloses this second fluid being immiscible with the first. (Column 7, lines 59-60)

Columbus does not explicitly disclose a fluid interface port having a dead volume of less than a picoliter, or the port having a diameter larger than its depth.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Columbus et al by using thinner plate materials and smaller port diameters, as taught by Bjornson et al, because miniaturization of these devices (Columbus is directed to electrochemical analysis of biological fluids) would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

Whether the port diameter is substantially larger than its depth is a function of the thickness of plate materials and port diameter, selection of which lies within the level of ordinary skill in the art. Applicants' amendment relies upon recitations of relative size as bases for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

12. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 11 above, and further in view of Columbus. (US 4,426,451)

Columbus (US 4,302,313) and Bjornson et al disclose a combined method as described above in addressing claim 11.

Neither Columbus (US 4,302,313) nor Bjornson et al explicitly discloses disposition of a hydrophobic patch in the channel to form a pressure barrier (Claim 13).

Columbus (US 4,426,451) discloses using a hydrophobic surface to prevent fluid flow into a region of his device. (Column 8, line 54 - Column 9, line 22)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Columbus (US 4,302,313) by performing it in a device that uses a hydrophobic surface to control fluid flow, as taught

by Columbus (US 4,426,451), because Columbus (US 4,426,451) teaches its effectiveness in preventing flow to undesired areas of the device, which is required in the method of Columbus. (US 4,302,313; Column 14, lines 29-40)

13. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 9 above, and further in view of Kopf-Sill. (US 6,420,143)

Columbus and Bjornson et al disclose a combined method as described above in addressing claim 9.

Neither Columbus nor Bjornson et al explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a fluid encapsulant. (Claim 17)

Kopf-Sill discloses sealing a fluid reservoir in a microfluidic device with mineral oil in order to reduce evaporative losses. (Column 8, lines 25-30)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Columbus by adding a liquid encapsulant to the fluid inlet port to seal it after the fluid filling step, as taught by Kopf-Sill, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

14. Claims 16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 9 above, and further in view of Swierkowski.

Columbus and Bjornson et al disclose a combined method as described above in addressing claim 9.

Neither Columbus nor Bjornson et al explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a covering layer or adhered covering layer. (Claims 18 and 19)

Swierkowski discloses sealing fluid reservoirs in a microfluidic device with an adhesive film in order to reduce contamination and evaporative losses. (Column 2, line 67 - Column 3, line 9)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Columbus by covering the fluid inlet ports with an adhesive covering layer in order to seal them after the fluid filling step, as taught by Swierkowski, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

15. Claims 42, 43, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg in view of Bjornson et al and Howitz et al.

Relevant to claim 42, Sundberg et al disclose a method of introducing a fluid into a microchannel comprising forming a droplet of the fluid and introducing it to the channel via a fluid interface port. (e.g. Embodiment of Figures 2 and 3) Each port is

shown as having a depth equal to the sidewall thickness, and a diameter larger than its depth.

Relevant to claim 43, Sundberg et al disclose the fluid port comprising a second port arranged coaxially with the first, directly opposite. (Figures 2 and 3; Column 5, line 64 - Column 6, line 25)

Relevant to claim 61, Sundberg et al disclose forming the droplet on a droplet-carrying element. (Figure 2)

Relevant to claim 62, Sundberg et al disclose applying the droplet to the port with the droplet-carrying element.

Sundberg et al do not explicitly disclose the port having a dead volume of less than about one picoliter, the droplet being introduced through a virtual wall formed by a fluid already disposed within the channel, or the droplet being introduced to the virtual wall by the droplet-carrying element.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters.

Howitz et al disclose addition of droplets of fluid through a virtual wall into a channel already filled with a fluid.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Sundberg et al by using thinner plate materials and smaller port diameters, as taught by Bjornson et al, because miniaturization of these devices would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Sundberg et al by introducing the fluid via a virtual wall in the port into a channel already filled with fluid, as taught by Howitz et al, because it would allow facile dosing of additional liquids into the device. The menisci in such a device would be positioned in planes defined by the respective sidewalls, meeting the limitation to these features being "substantially coplanar".

Furthermore, claim 42 relies upon a size limitation as a basis for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

16. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al, Bjornson et al, and Howitz et al as applied to claim 42 above, and further in view of Swedberg et al.

Sundberg et al, Bjornson et al, and Howitz et al disclose a combined method as described above in addressing claim 42.

None among Sundberg et al, Bjornson et al, or Howitz et al explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Sundberg et al, Bjornson et al, and Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

17. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Swedberg et al.

Howitz et al disclose a method as described above in addressing claim 42.

Howitz et al do not explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

18. Claims 57, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Sundberg et al.

Howitz et al disclose methods as described above in addressing claim 42 and 56.

Howitz et al do not explicitly disclose causing fluid motion by electric fields (Claim 57), forming the droplet on a droplet-carrying element (Claim 61), or introducing the droplet to the virtual wall on a droplet-carrying element. (Claim 62)

Sundberg et al disclose fluid motion being caused by application of an electric field (Column 6, lines 26-33), formation of droplets on a carrying element prior to introduction to a channel (Figure 2), and introduction of the droplet to the port via the carrying element. (Column 5, lines 32-34)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by causing fluid

motion by application of an electric field, as taught by Sundberg et al, because it is a reliable means of causing fluid motion in a channel.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by forming droplets on pins and introducing the droplets to the ports on these pins, as taught by Sundberg et al, because it is a controllable, reliable fluid transfer means.

Response to Arguments

19. Applicant's arguments filed 19 October 2005 have been fully considered but they are not persuasive.

Applicant argues that the amendments to (a) having a port with diameter greater than its depth and (b) a virtual wall having a meniscus that is coplanar with the sidewall in which it is formed distinguish the claims from the prior art of record. The Examiner respectfully disagrees.

In all cited documents (e.g. Howitz et al, Columbus '451, Heller et al), the menisci that form in the cited inlet ports can be accurately described as substantially coplanar with the sidewalls in which they are formed.

Limitations to respective dimensions without a difference in operation cannot be the basis for patentability. As cited above, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that changes in size alone do not provide patentability.

Regarding the application of the Columbus '313 reference, Applicants argue that the reference does not teach the limitations regarding the dead volume and the diameter of the port. The Examiner agrees that Columbus alone does not teach these limitations. However, the Examiner considers that the picoliter (or less) dead volume would result from the miniaturization of the dimensions of the device of Columbus et al, the feasibility of which is demonstrated by Bjornson et al, who demonstrated micron scale ports in thin plates as described above. As in the case of Howitz et al, the dead volume associated with these ports would vary depending on fluid and device properties, which would be a matter of selection to one having ordinary skill in the art.

In response to Applicant's detailed description of what the term "virtual wall" is intended to denote, the Examiner fails to see a patentable distinction between the structure and method explicitly described in the instant claims and that described by the prior art as described above.

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

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